

REMARKS**Status of Claims**

Claims 1-24 are pending after entry of this paper. Claims 14-24 have been rejected and claims 14 and 24 have been objected. Claims 1-13 have been previously withdrawn. Applicants reserve the right to pursue withdrawn claims in a divisional or continuing application.

Claims 14 and 24 have been amended to replace the terms "mercapt" and "function" with the terms "mercapto" and "functional," respectively in accordance with the Examiner's suggestions (See Office Action – pages 2-3).

No new matter has been introduced by these amendments. Reconsideration and withdrawal of the pending rejections in view of the above claim amendments and below remarks are respectfully requested.

Response to Claim Objections

Claims 14 and 24 have been objected to because of informalities. The Examiner has indicated that the word "mercapt" should read -- mercapto--, and the phrase "second function group" should read -- second functional group --. In order to facilitate the examination of the instant application, claims 14 and 24 have been amended in accordance with the Examiner's suggestions as presented above.

Response to Rejections under 35 U.S.C. §103

Claims 14-17 and 19-24 have been rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 5,688,642 to Chrisey et al. ("Chrisey") in view of U.S. Patent

Publication No. 2002/0039742 to Iwaki et al. ("Iwaki"), and in further view of U.S. Patent Publication No. 2002/0198314 to Meisenburg et al. ("Meisenburg"). The Examiner maintains that Chrisey teaches a method of immobilizing a probe on a solid phase carrier that allegedly includes the steps of providing a DNA oligomer having a thiol group with a linker molecule, providing a silica substrate with an amino silane coating, imparting the probe to the immobilization substrate, binding of the first functional group of the probe with the second function group of the substrate (Office Action – pages 4-5). The Examiner admits that Chrisey is silent about the direct bonding between DNA with mercapto group and the substrate with the amino group via ionic bond (Office Action – pages 5 and 8), which is allegedly made obvious in view of Iwaki. Applicants respectfully disagree.

Contrary to the Examiner's contention, the combination of prior art references does not teach each and every element of the claimed invention, either explicitly or inherently, as presented in the independent claims 14 and 24. The Examiner attempts to reach the claimed method by pointing to Figure 3 of Chrisey for the disclosure of the mercapto group and to Figure 4 of Chrisey for the disclosure of the amino-functional group.

As the Examiner is well aware MPEP 2141 states that:

A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. W.L. Gore & Associates, Inc. v. Garlock, Inc., 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984) (emphasis added).

Figure 3 of Chrisey shows the binding of a DNA oligomer with a substituted mercapto group at 3' position to an organosilane with either exposed functional amino group or an amino group with the heterobifunctional crosslinker, i.e., SMPB (succinimidyl 4-(p-maleimidophynyl)butyrate). Figure 3 clearly demonstrates that the DNA oligomer with a substituted mercapto group covalently binds to the heterobifunctional crosslinker. In fact, any

electrostatic interactions are undesirable according to Chrisey, whenever a DNA oligomer with a substituted mercapto group is utilized (See Example 9), because any oligomer that electrostatically interacts with the substrate is removed by washing. In essence, Chrisey teaches away from using the oligonucleotide with a mercapto group for anything else but the covalent bonding, contrary to the Examiner's contention. Figure 4 on the other hand discloses electrostatic interactions between the amino group of the organosilane coating and a phosphodiester backbone of the DNA. One skilled in the art would not consider a phosphodiester backbone of DNA as equivalent to a DNA oligomer with a substituted mercapto group at either 3' or 5' position. Contrary to the Examiner's contention, the disclosures of Figure 3 and Figure 4 are not combinable, because they refer to two distinct methods of linking DNA oligomer with the substrate, *i.e.*, covalent vs. electrostatic. One skilled in the art would not pick and choose various components of the Chrisey disclosure to achieve the claimed method and furthermore, Chrisey disclosure actually teaches away from the claimed invention.

Furthermore, the Examiner looks to Iwaki and contends that the direct bonding between mercapto group and amino group via ionic bond was known in the art as taught by Iwaki (Office Action – page 8). To support this notion, the Examiner points to Examples 4-6. However, applicants respectfully assert that Examples 4-6 discloses a method of fixing the probe molecule onto the plate by electrostatic bonding, where the probe molecule is an oligomeric DNA having a fluorescent label Cy5 (cyanine dye). The electrostatic interaction similarly to Chrisey (see Figure 4) occurs between the phosphodiester backbone of the oligomeric DNA and the amino group of the organosilane compound and not between the mercapto group on the DNA oligomer and amino group on the organosilane. Furthermore, Iwaki teaches that the electrostatic

interaction requires a thickening agent, otherwise the retention ratio after washing is very low (See Table 2 and para. [0102]).

The Examiner further points to para. [0008] to support the notion that Iwaki teaches that the surface of solid phase carrier has the amino group and the DNA oligonucleotides have the mercapto group (Office Action – page 8). Applicants again respectfully wish to remind the Examiner that “[a] prior art reference must be considered in its entirety... including portions that would lead away from the claimed invention” (MPEP 2141). In fact, the disclosure in para. [0008] of Iwaki would clearly lead away from the claimed invention, because the synthesized oligonucleotide probe with a mercapto group and the surface of the solid carrier with an amino group are explicitly disclosed by Iwaki to be used in covalent bond formation, whereas the claimed invention is directed to a coupling without any covalent bonding. Applicants respectfully assert that one skilled in the art would be further encouraged to use the mercapto group and amino group only for covalent coupling based on the combined disclosure of Chrisey and Iwaki. In essence, both Chrisey and Iwaki teach away from using the mercapto group and amino group to form an ionic bond, contrary to the Examiner’s contention.

Finally, Examiner contends that Iwaki teaches that solid phase carrier is coated with aminosilane and contacted with DNA molecule carrying appropriate anionic groups forms an electrostatic binding (Office Action – page 8). The Examiner further points to Meisenburg to support that the mercapto group is known in the art as an anionic group.

As the Examiner well aware

[a] reference itself must have an enabling disclosure to be used as a proper reference. Section 102(b) of 35 U.S.C. and its predecessor statutes have been interpreted as requiring the description of the invention in a publication to be sufficient to put the public in possession of the invention. *Ex parte Gould*, 231 U.S.P.Q. 943 (B.P.A.I. 1986).

An artisan would not have sufficient guidance from reading the combination of cited art to select the appropriate anionic groups, e.g., mercapto group in order to produce the claimed method. Moreover, a significant amount of undue experimentation would be necessary in order to ascertain which anionic group would be appropriate in order to arrive at the claimed electrostatic bonding.

In light of the above arguments, the applicant asserts that neither Chrisey, nor Iwaki alone, or the combination thereof satisfies all of the elements of the claimed method. Iwaki does not remedy the deficiencies in the method described by Chrisey, and in fact both Chrisey and Iwaki teach away from using the mercapto group with the amino group to form non-covalent ionic bond. Therefore, the combination of Chrisey and Iwaki does not make obvious the claimed invention. The applicant respectfully requests reconsideration and withdrawal of the 35 U.S.C. §103(a) rejection of claims 14-17 and 19-24 in view of the aforementioned remarks and amendments to the claims.

Claims 14 and 18 have been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over U.S. Patent No. 5,688,642 to Chrisey et al. ("Chrisey") in view of U.S. Patent Publication No. 2002/0039742 to Iwaki et al. ("Iwaki"), as applied to claim 14, and further in view of U.S. Patent No. 5,688,642 to McGovern et al. ("McGovern"). Applicants respectfully disagree.

Claim 14 is directed to a method of immobilizing a probe that is specifically bindable to a target substance. As demonstrated above, the combination of Chrisey and Iwaki even with Meisenburg does not teach each and every element of the claimed invention as disclosed in claim 14. The McGovern reference, on the other hand, does not compensate for the shortcomings of Chrisey and Iwaki.

Applicants assert that the combination of Chrisey, Iwaki and McGovern does not teach, disclose, or suggest the method claimed in claim 18. Specifically, applicants respectfully assert that McGovern does not cure the deficiencies of Chrisey and Iwaki noted in the previous subsection. Thus, applicants contend, that the proposed combination of references fails to teach, disclose, or suggest all of the claim elements of applicant's invention. For at least these reasons, reconsideration and withdrawal of the rejections of the claims 14 and 18 are respectfully requested.

Dependent Claims

The applicants have not independently addressed all of the rejections of the dependent claims. The applicants submit that for at least similar reasons as to why independent claims 14 and 24 from which all of the dependent claims 15-23 depend are believed allowable as discussed *supra*, the dependent claims are also allowable. The applicants however, reserve the right to address any individual rejections of the dependent claims and present independent bases for allowance for the dependent claims should such be necessary or appropriate.

Thus, applicants respectfully submit that the invention as recited in the claims as presented herein is allowable over the art of record, and respectfully request that the respective rejections be withdrawn.

Based on the foregoing remarks and arguments, the applicants respectfully request reconsideration and withdrawal of the pending rejections and allowance of this application. The applicants respectfully submit that the instant application is in condition for allowance. Entry of the arguments presented herein and an action passing this case to issue is therefore respectfully requested. In the event that a telephone conference would facilitate

examination of this application in any way, the Examiner is invited to contact the undersigned at the number provided. Favorable action by the Examiner is earnestly solicited.

AUTHORIZATION

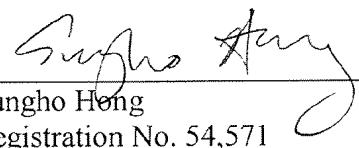
The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. **13-4500**, Order No. 1232-5579.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. **13-4500**, Order No. 1232-5579.

Respectfully submitted,
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